Direct Puncture and Sclerotherapy with Sotradecol®

Orbital Lymphatic Malformations

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Key words: lymphatic malformations, orbit, alcohol injections, sclerotherapy

Summary

We evaluated sclerotherapy in the treatment of orbital lymphatic malformations.

Six consecutive patients with unilateral orbital cystic masses and recurrent episodes of orbital swelling were included in this retrospective study. All have been treated with percutaneous puncture and injection of Sotradecol (sodium tetredecyl sulphate) under radiographic guidance, on one or more occasions.

Reduction of orbital mass volume was documented clinically and radiologically within a few weeks in all cases. There was total regression of proptosis in three instances. There were no immediate complications. One subject suffered a presumably coincidental orbital hemorrhage two weeks after treatment. Follow-up times ranged between six months and four years.

Sotradecol sclerotherapy appears to be a useful adjunct to the therapeutic arsenal for orbital lymphatic malformations.

Introduction

Vascular lesions are either tumors or malformations [8]. Vascular malformations are arterial, capillary, venous, arteriovenous or mixed. Lymphatic malformations or lymphangiomas also belong to vascular malformations. According to the International Society for the Study of Vascular Anomalies (ISSVA) (11th Annual Meeting in Rome 1996), there may also be mixtures of venous and lymphatic malformations.

Since 1990 we have treated 150 patients with venous malformations in various locations, initially by injecting ethanol and later sodium tetradecyl sulphate, Sotradecol® (Elkins-Sinn, Inc, Cherry Hill, NJ, USA) directly into the venous cavities (sclerotherapy). Using digital subtraction fluoroscopy, we guided the needle and observed the distribution of the contrast medium after injection [1, 9, 11].

The local toxic effect of concentrated ethanol is related to its protein denaturing and hygroscopic properties [1]. When Sotradecol is injected intravenously it produces sludging of erythrocytes and subsequent thrombosis followed by permanent obliteration of the vessels by organized thrombosis (intimal necrosis, adventitial fibrosis and luminal collapse) [7, 8, 9]. Our experience is that ethanol is more efficient than Sotradecol but carries a higher risk of complications, mostly necrosis of soft tissue [1, 9, 11].

Since 1994 we have also treated 15 patients with lymphatic malformations in different locations with good results (unpublished). We present here our first experience of treating lymphatic malformations in the orbit by direct puncture and sclerosing with Sotradecol.

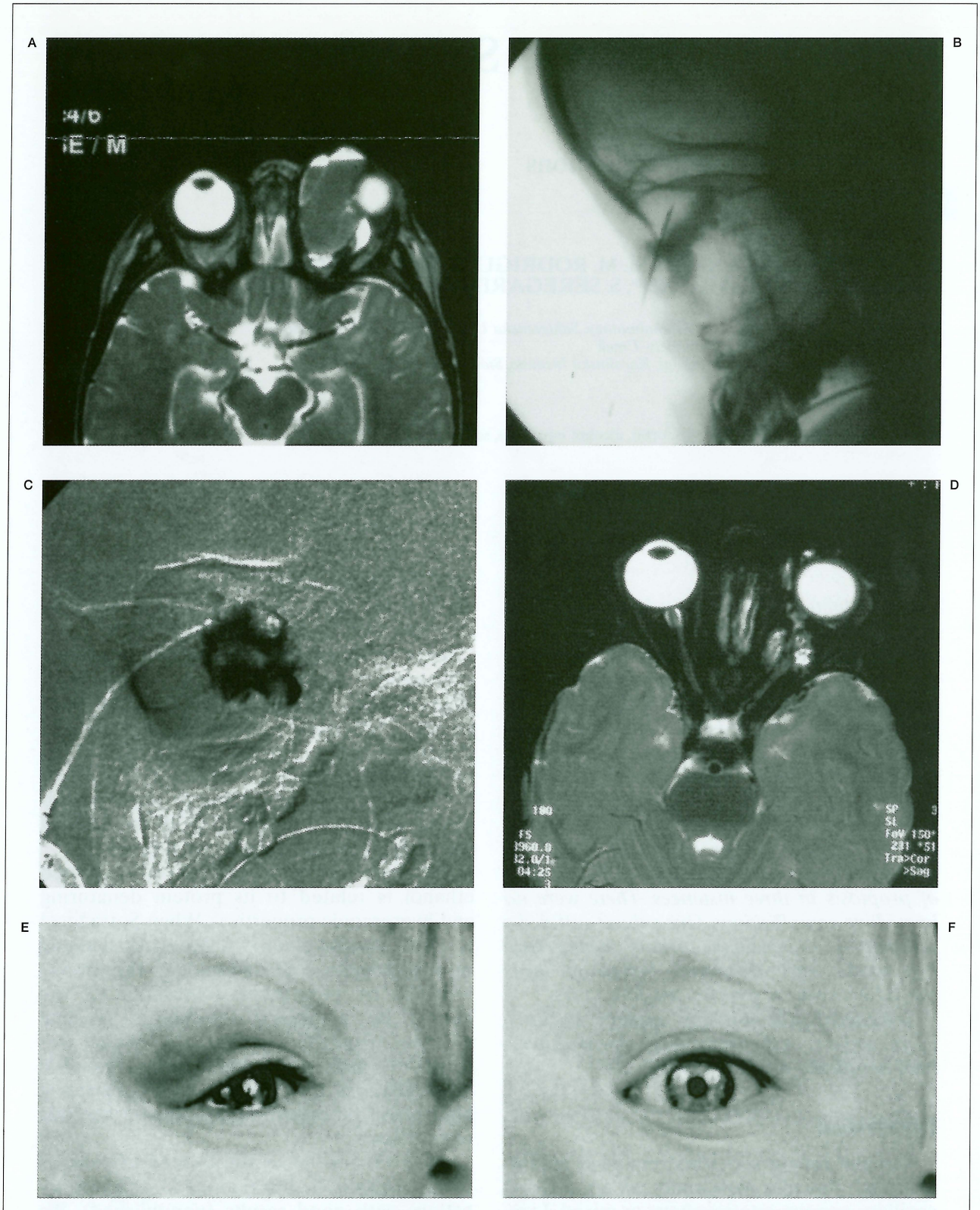

Figure 1 (Case 6) A small girl with moderate exophthalmos caused by a large lymphatic malformation. MRI before treatment showed large masses in the left orbit (A). Needle in position in the orbit (B). Road map of Sotradecol injected in the lymphatic mass medially in the left orbit (C). Compare A and B. Six months after the first injection the lymphatic masses are almost invisible at MRI (D). Compare A. Photographs before (E) and after treatment (F).

Material and Methods

Six patients with a clinical diagnosis of lymphangioma and MRI findings of a mass lesion in the orbit were referred to us after years of problems with an expanding processes in the orbit, often exaggerated during viral infections. Based upon clinical findings and MRI examinations, the lesions in the orbit were punctured directly under general anesthesia. The punctures were guided by radiological fluoroscopy with digital subtraction and the so-called roadmap technique to avoid deposition of Sotradecol outside the lymphatic cavities. After the treatment, patients were given 2 mg betamethasone (Betapred, Glaxo Wellcome AB, Sweden) twice a day for two days to counteract swelling in the orbit.

1) Diagnostic radiology

a) *Roadmapping* is a digital subtraction technique. This technique implies that a first x-ray image is reversed in the x-ray unit's computer; black turns white and vice versa. This reversed image (the mask) is superimposed on the following normally displayed images, thereby creating a "blank" image where all image pixels have the same value. Bone and other structures that normally obscure the image are thus made invisible and the only things seen are "new" contrasting agents introduced in the field of vision like needles, catheters and x-ray contrast (figure 1). This technique demands the patient's stillness since motion gives incongruity between the mask image and the following images and severe artefacts.

b) *Angiography* was performed in two cases in order to disclose any other vascular malformations. An arterial component is best treated transarterially. With experience, we have decreased the number of selective angiograms although this is a simple procedure with a complication rate of less than 0.5%.

c) *MRI*: The differential diagnosis between lympathic and venous malformations and hemangiomas is not possible with MRI[8]. However, T2-weighted MR-images are of tremendous help in mapping the venous or lymphatic malformations (figure 1, 2, 3). We use the MR-images as a map to direct the tip of the cannula into the cavities in the orbit (figure 1).

2) Interventional radiology (sclerosing procedure)

General anesthesia is mandatory not only because of the pain and discomfort the sclerosing procedure may cause, but also because it is absolutely essential that the patient be immobile when using digital subtraction. After puncture, backflow of fluid or blood in the syringe may occur. Thereafter, a small amount of contrast medium is injected. On the monitor we can verify that the tip of the needle is in a cavity (figure 1, 2). If the tip of the needle is in the correct position, we inject the Sotradecol in a suitable amount, usually about 0.5 – 2 cc. Sometimes several punctures are done but we try to limit the amount of Sotradecol injected.

3) Postoperative care

The eyelids are often swollen, making it difficult to test vision. The eyelid swelling comes to a maximum during the first or second day. We do not judge the results of the sclerosing treatment before 4-6 weeks, the time required for phagocytosis of the debris and resorption of swelling.

Case reports

Case 1. The patient was a twenty-six-year old woman with a history of many years of eye protrusion and masses in the right orbit and the right side of the face. She had had several surgical resections years before. Microscopical examination demonstrated lymphatic tissue. MRI examinations showed large masses in the orbit and the right side of the face.

In February 1997 we started with punctures and injections of Sotradecol, initially in the orbit, later also in the face. The patient noted improvement in the orbit which was also recorded on MRI.

She became pregnant during 1998 and delivered a healthy baby in July 1999. We will continue the treatment after termination of breastfeeding.

Case 2. This ten-year-old girl had protrusion of the left eye at one year of age. Orbital hemorrhage occurred once, prompting surgical evacuation. She has also had infections and abscesses. Vision decreased to 0.3. MRI demonstrated masses in the left orbit.

Punctures and injections of Sotradecol start-

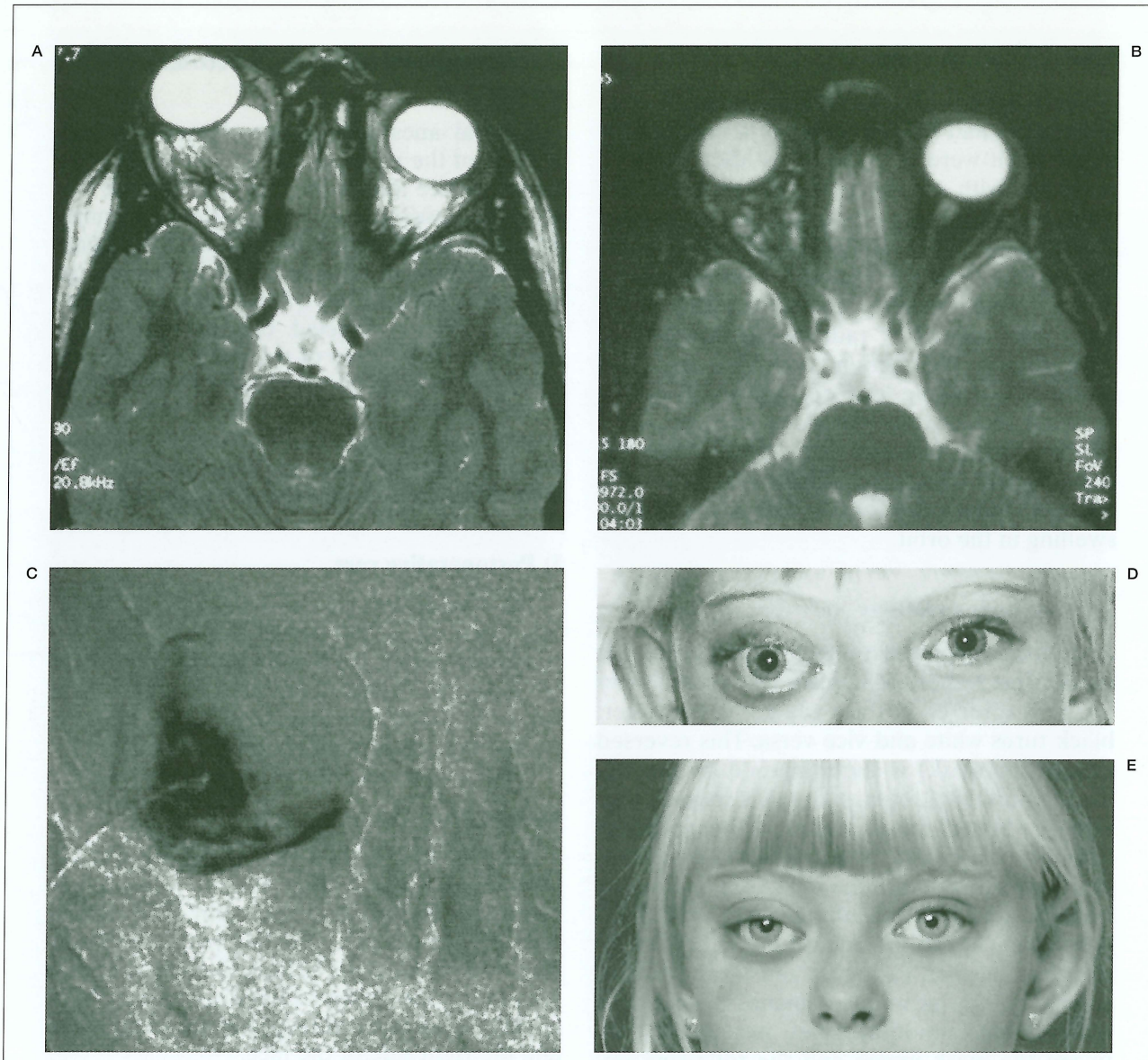

Figure 2 (Case 5) Moderate exophthalmos caused by masses in the right orbit, clearly visible on MRI before treatment (A). After one procedure the MRI showed small remnants four months later (B). Injection needle in position at Sotradecol treatment (C). Photograph of the eye before (D) and after treatment (E).

ed at the age of ten years. Thick yellow and partly hemorrhagic fluid was extracted. The last treatment was performed one and a half years later. She now has an almost normal exterior. MRI showed regression.

Case 3. (figure 3) This patient was a seventeen-year-old male with a ten-year history of eye protrusion and a clinical diagnosis of lymphangioma. Lateral decompression was attempted at the age of eight years. After a period of improvement, the proptosis increased again dramatically.

In August 1999 we punctured the cavities demonstrated on MRI and injected Sotradecol. He noted improvement but two weeks later he had an orbital hemorrhage and lateral decompression was necessary. Sclerotherapy was repeated in October 1999. A third treatment was planned in November but at that time the eye had a normal position. A new MRI examina-

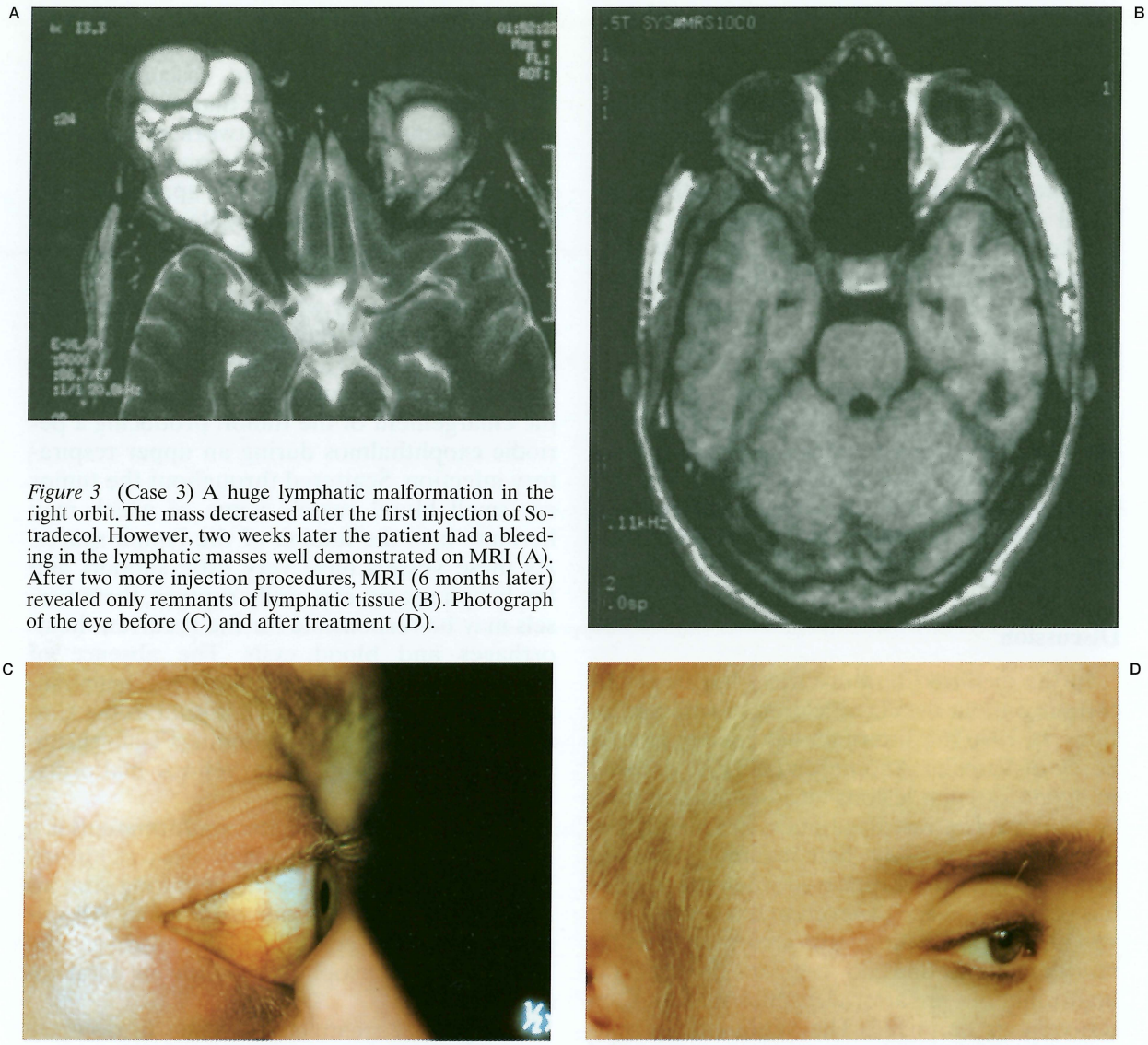

Figure 3 (Case 3) A huge lymphatic malformation in the right orbit. The mass decreased after the first injection of Sotradecol. However, two weeks later the patient had a bleeding in the lymphatic masses well demonstrated on MRI (A). After two more injection procedures, MRI (6 months later) revealed only remnants of lymphatic tissue (B). Photograph of the eye before (C) and after treatment (D).

tion has demonstrated no exophthalmos but scattered remnants of lymphatic tissue.

Case 4. This six-year-old girl had had moderate protrusion of the left eye since birth. In 1997 there was a sudden increase in proptosis with a cardiac vagal reaction. Lateral decompression was necessary. Histopathology revealed lymphatic malformations. We treated her once with puncture and sclerosing in September 1999. Another treatment was planned for November but protrusion was no longer noted. MRI examination later showed regression of lymphatic masses.

Case 5. (figure 2) This patient was a seven-year-old girl with a clinical history of lymphatic malformations since two years of age. The exophthalmos increased step-by-step, often in connection with viral inflammatory episodes. MRI examination initially demonstrated large cavities, which were injected.

The large cavities had later changed to several small cystic cavities. We did four punctures in one procedure and injected Sotradecol. MRI-examination four months after the first injection revealed only small spots of lymphatic tissue were seen.

Case 6. (figure 3) This two-year-old girl had a lymphatic mass in the left orbit. Sudden growth at one year of age caused dislocation of the eye and disturbance of the eye-reflex. Sanguineous fluid was extracted. MRI revealed bulging masses. Direct puncture and instillation of Sotradecol was done three times with an interval of six weeks. The exophthalmos disappeared and the exterior was normalized. MRI showed minimal remnants of lymphatic masses.

Results

We observed total regression of proptosis in three cases (case 3, 4 and 6) and almost total in one (case 2). Obvious reduction of the masses in the orbit was noted in cases 1 and 5. We had no obvious immediate complications. However, a hemorrhage occurred two weeks after sclerotherapy in case 3 (figure 3).

Discussion

In the medical literature there has been uncertainty about the classification of vascular lesions. In 1996 the International Society for the Study of Vascular Anomalies (ISSVA) decided to divide vascular lesions into tumors and malformations. The vascular tumors are mainly hemangiomas. Capillary hemangiomas involute and have usually disappeared when the patient has reached the age of seven to ten years [7,8]. The vascular malformations are errors of vascular morphogenesis and do not vanish. Vascular malformations are arterial, capillary, venous, arteriovenous or mixed. The venous malformations consist of malformed venous cavities or widened channels, sometimes large cavities, sometimes multi-cystic masses. Blood flow in venous malformations is slow [1,4,7,8,9,11]. It can be difficult to differentiate venous malformations clinically from hemangiomas [4]. Venous or lymphatic malformations do not disappear. They do not involute.

By ISSVA consensus, lymphatic lesions (sometimes called lymphangiomas) belong to the vascular malformations.

We try to avoid the old term lymphangioma because it indicates "tumor". The terms lymphatic or venous-lymphatic malformations are more correct. At the 13th meeting of the Interventional Society for the Study of Vascular Anomalies (ISSVA) in Montreal, in 2000, the name lymphatic malformations was preferred.

Snow Jones and Jakobiec 10 characterized lymphangiomas as "delicate vascular spaces filled with clear fluid rather than blood. In the orbital lesions there is a network of empty or bloodless spaces lined by flattened endothelial cells. Endothelial spaces do not appear to have any pericytes or smooth muscular cells in their wall. The stroma between the lymph spaces is hypocellular and loose. There are foci of lymphoid cells, some of which may exhibit follicle formation with germinal centers. It is presumed that these are able to react in the course of the viral infections and contribute to the enlargement of the tumor, producing a periodic exophthalmos during an upper respiratory infection. Scattered throughout the tumor are small blood vessels, some of which may herniate into the lumina of the lymph spaces. As these vessels have very little support and the lymph spaces can easily rupture, these vessels may be responsible for the recurrent hemorrhages and blood cysts. The absence of smooth muscles in the walls of the lymphangioma is a salient point, in addition to the clinical and histopathological findings, against subsuming these lesions with venous malformations."

Hemorrhage in lymphatic malformations is a not uncommon event in their natural history. They commonly increase in size during viral infections [10]. This is also our experience. All our six patients had episodes of hemorrhage and had increasing exophthalmos during viral infections.

The goal of treatment must be to decrease the mass effect in the orbit and to prevent episodes of bleeding in the future.

If there is a venous component in the malformation, we also believe in the treatment with Sotradecol. This is based on experience [1,9,11]. We have had good results when treating lymphatic malformations in other parts of the body as well, except for two cases with small cystic lymphatic lesions. Sotradecol does not penetrate into all the small cysts.

In treating venous malformations we observed complications. Alcohol deposited outside the venous cavities caused soft tissue necrosis in five patients. This has only happened in one case with Sotradecol. After the injection of sclerotic agents, there will be an inflammatory reaction in the tissue in the vicinity.

In one patient with a venous malformation in the face including the orbit, some Sotradecol inadvertently passed into the orbit, causing swelling with gross exophthalmos, which resulted in blindness. This complication has not occurred while deliberately injecting into the orbit. One obviously has to sclerose this kind of orbital masses very carefully to avoid too much swelling.

In 1999 Wojno published his experience of injecting Sotradecol into three patients with orbital lymphangiomas in the eyelid [12]. The pathology of lymphatic malformations is well presented although the author prefers the word lymphangioma and also writes about "the tumor". He presented promising results of the treatment and mentioned scars after multiple operations as a disadvantage while an inflammatory reaction to the injection of Sotradecol could be an advantage.

Although the treatment in our six patients so far has been successful, it is too early to judge the final outcome. The patients need to be followed for a long time. Although we do not fully know the pathology, we feel that treatment with direct puncture using high quality radiological equipment and injecting Sotradecol is promising.

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